

Appl. No. 09/486,715  
Amendment dated: July 30, 2003  
Reply to OA of: March 31, 2003

### **REMARKS**

Applicants have amended the claims to more particularly define the invention taking into consideration the outstanding Official Action. In addition, claims 15-29 have been added to the application to include claimed subject matter that was deleted at the time of entering national phase to reduce the initial filing fee. These claims add the subject matter of multiple dependent claims 9, 10 and 12 as originally filed. Applicants most respectfully submit that all the claims now present in the application are in full compliance with 35 U.S.C. 112 and are clearly patentable over the references of record.

Applicants note the Examiner's comments with respect to the response to the Restriction Requirement. While Applicants do not agree that restriction is appropriate, the non-elected invention has been canceled from the application without prejudice or disclaimer and will be made the subject of a divisional application.

Applicants have amended claims 6 and 8 in the present amendment. In the amendment to claim 6, part c) "a multiwavelength spectrophotometric detector for... producing data at more than one wavelength relating to at least one chemical or physical characteristic of the fluid..." has been added to the claim. Also, claim 8 has been amended to specify that "...the spectrophotometric detector is a scanning ultraviolet or visible range spectrophotometer". Basis for these amendments can be found at page 9, lines 18-23, of the specification (as published), which explains the data treatment required in order to derive pKa values from multiwavelength absorbance spectra. Also, page 17, line 34 to page 18, line 6, describes the data collection from a multiwavelength scanning spectrophotometer which collects data at 256 wavelengths, at 480 data points per wavelength (p. 18, lines 21-24) and page 28, lines 13-18, discusses the use of data collected at up to twenty separate wavelengths. Other examples in the specification utilize data collection at 4 different wavelengths. Applicants most respectfully submit that all of the claims now present in the application are in full compliance with 35 USC 112 and are clearly patentable over the references of record.

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The rejection of claims 10 and 12 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been carefully considered but is most respectfully traversed.

The Examiner urges that claim 10 recites a plurality of samples while the parent claim recites "the fluid". It is said that it is not clear that if a plurality of samples mean a plurality of fluids or these are different samples of the same fluid. One of ordinary skill in the art would appreciate that the automated sample delivery device adapted to deliver a plurality of samples successively delivers these into the common channel and in element c of the parent claim, the reference is to a fluid in the detection zone. Accordingly, it is most respectfully requested that this aspect of the rejection be withdrawn.

The rejection of claim 12 has been carefully considered but is most respectfully traversed. The rejection states that claim 12 provides for the use of an analytical device, but since the claim does not set forth any steps involved in the method process it is unclear what method process Applicant intends to claim. However, as noted in the Official Action with respect to the restriction, the apparatus of claim 12 is for high-throughput determination of pKas and is not a method but an apparatus claim and it would not be expected to have a method step as would be appreciated by one of ordinary skill in the art. Accordingly, it is most respectfully requested that this aspect of the rejection be withdrawn.

The rejection of claims 6-10 under 35 U.S.C. 102(b) as being unpatentable over Surjaatmadja has been carefully considered but is most respectfully traversed.

Applicants wish to direct the Examiner's attention to MPEP § 2131 which states that to anticipate a claim, the reference must teach every element of the claim.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is

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contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed Cir. 1989). The elements must be arranged as required by the claim, but this is not an *ipsissimis verbis* test, i.e., identity of terminology is not required. *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed.Cir. 1990).

In the Official Action it is urged that Surjaatmadja discloses an apparatus for automatic titration, comprising at least two input ports in fluid communication with a common channel, a detection zone having an input in fluid communication with the common channel and the output, a color detector for detecting the color of the fluid and control means connected to continuous flow type metering pumps to vary the composition of the fluid continuously and linearly.

The present invention relates to apparatus which may find use in a number of analytical techniques, as set out in the specification, amongst which probably the most important is the determination of the pKas of ionizable groups in compounds, particularly the first determination of previously unknown pKas. The pKa of an ionizable group is the pH at which the group is 50% ionized. If the compound under examination possesses a chromophore that changes with the compound's ionization state, the absorbance of electromagnetic radiation at the particular wavelength characteristic of the chromophore will also change to follow the transition from the neutral to the ionized forms of the molecule as the pH is varied during a titration.

Using traditional apparatus such as a fixed wavelength colorimeter (as described in the '509 citation) only known compounds can be investigated, as one needs to know in advance the color change which will need to be observed (which corresponds to the wavelength at which data should be recorded). Thus, Surjaatmadja describes (column 3, final paragraph) how his system may be used to determine the presence of various known analytes in samples of well water. As each sample is processed, the appropriate reagent is selected to perform the titration and, depending on the (known) pH transition at which the reaction will be completed, the appropriate color-changing indicator is chosen. Then the color detector collects data at a visible wavelength for that indicator.

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When the indicator's color change occurs, the titration has reached or passed through a particular pH that may show that all the analyte has been reacted with the titrant. Such a system could also be used to determine the concentration of the known analyte, by determination of the "equivalence point" as is describe din column 3, first paragraph, in relation to continuous operation of the Surjaatmadja apparatus.

By contrast, the presently claimed apparatus incorporates a multiwavelength detector and collect data at more than one wavelength. This allows unknown compounds to be tested because absorbance changes in those compounds are observed at each of the wavelengths. The wavelength(s) at which the biggest absorbance changes are detected can then be selected for use in determining the pKa(s) of ionizable group(s) in the compound with the greatest sensitivity. It is therefore unnecessary to know the identity or physicochemical characteristics of the compound in advance in order to utilize the apparatus of the presently claimed invention, which makes it particularly valuable in the pharmaceutical industry where (as set out in the paragraph bridging pages 2 and 3 of the specification) large numbers of new, uncharacterized compounds requiring analysis are constantly being generated.

Thus, the Surjaatmadja '509 reference does not describe or teach an apparatus according to the current claims. Indeed the apparatus described in the '509 reference could not operate in the way described in the current specification and could not be utilized for the high-throughput determination of pKas (and does not claim to do so). It is therefore submitted that the claims submitted herewith are novel and non-obvious in view of this reference. Accordingly, it is most respectfully requested that this rejection be withdrawn.

The rejection of claim 11 as obvious over Surjaatmadja in view of Garrison has been carefully considered but is most respectfully traversed. Applicants most respectfully submit that the Garrison reference discusses the use of an autosampler with a potentiometric titration apparatus. As the limitations from claims 6 and 10, are included in claim11 and are novel over Surjaatmadja, the combination of an autosampler with the Surjaatmadja apparatus cannot lead to the apparatus of claim 11

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and this claim is also non-obvious in view of Surjaatmadja alone or in combination with Garrison. Accordingly, it is most respectfully requested that this rejection be withdrawn.

In view of the above comments and further amendments to the claims, favorable reconsideration and allowance of all of the claims now present in the application are most respectfully requested.

Respectfully submitted,

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